Remarks/Arguments

The foregoing amendments in the specification and claims are of formal nature, and do not add new matter.

Prior to the present amendment, claims 39-58 were pending in this application and were rejected on various grounds. Claims 48 and 53 have been cancelled without prejudice. The rejection to the remaining claims is respectfully traversed.

Priority

2) The Examiner has concluded that applicants are entitled only to the filing date of the present application which is July 11, 2001. As it will be apparent from the rest of the response, Applicants rely on the gene amplification assay results (Example 92) to establish substantial and specific asserted utility for the polypeptide PRO343. These results were first disclosed in international application PCT/US99/30095 (P2509R1), filed December 16, 1999 and published as WO 00/37640 on June 29, 2000. Support is present at least at pages 133-137, pages 154-155 and pages 116-121 of the WO 00/37640 publication. Accordingly, the present application is entitled to the effective filing date of December 16, 1999.

Specification

3) The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

In addition, amendments to the specification have incorporated the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent."

Accordingly, Applicants believe that all objections to the specification has been overcome.

Claim Rejections - 35 USC § 101

4a) Claims 39-58 were rejected under 35 U.S.C. 101 allegedly "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility." The Examiner specifically noted that "the specification provides no working examples as to the activity of the PRO343 polypeptide, and one of ordinary skill in the art would not be able to predict what activity would be possessed by the protein of the instant application."

The rejection is respectfully traversed.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for the PRO343 polypeptide.

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 9 (pages 230-234 of the specification), including primary lung cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification. PRO343 showed approximately 2-3-fold amplification in 6 primary lung tumors, approximately 4-fold amplification in 3 primary lung tumors, approximately 8-fold amplification in 2 primary lung tumors, approximately 2-3 fold amplification in 13 primary colon tumors and approximately 4-9 fold in 5 primary colon tumors.

In assessing the value of these data, the Examiner notes that: "it does not describe the significance of this expression, nor does it compare the expression of PRO343 in normal lung

and colon tissues to the expression of said protein in lung and colon tumors or tumor cell lines." As a negative control, DNA was pooled from the cells of ten normal healthy individuals (page 222, lines 34-36). Although, the results are based on comparison with normal lung and colon tissues, using mixed DNA as a reference is customary in gene amplification studies.

Regarding the significance of the gene amplification results done using real-time quantitative TaqMan™ PCR, as discussed above, PRO343 showed approximately 2-3-fold amplification in 6 primary lung tumors, approximately 4-fold amplification in 3 primary lung tumors, approximately 8-fold amplification in 2 primary lung tumors, approximately 2-3 fold amplification in 13 primary colon tumors and approximately 4-9 fold in 5 primary colon tumors. The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ real-time PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The Declaration also confirms that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO343 is a diagnostic marker of human lung and colon cancer. It is, of course, true that further research might be needed to develop PRO343 into a diagnostic product. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that PRO343 lacks patentable utility. Indeed, the gene amplification results for PRO343 are way above figures that are considered significant and clearly support the role of PRO343 as a tumor marker.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility in viewed "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO343 is a diagnostic marker of lung and colon cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based are not inconsistent with the logic underlying the assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large

percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections - 35 USC § 112

4b-d) Claims 39-58 were rejected under 35 U.S.C. 112, first paragraph allegedly "because one of skill in the art would not know how to use the claimed invention and since the specification does not reasonably convey to one skilled in the art that the inventors had possession of the claimed genus at the time of filing." Further, claims 39-44, 51-52 were rejected allegedly "because the deposit of ATCC accession number 209481 must be readily available to the public."

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that undue experimentation is not required of the skilled artisan to use the claimed invention and that the specification discloses a substantial, specific and credible utility for the PRO343 polypeptide or antibodies against it. This specific utility is now recited in the rejected claims, which is believed to overcome the present rejection. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims under this section.

Regarding the rejection to the claimed genus, without admitting to the propriety of this rejection and solely in the interest of expediting prosecution in this case, the present claim amendments add the recitation that the nucleic acid molecules "encode polypeptides associated with the formation or growth of lung or colon tumor." The specification provides ample enablement for the polypeptides defined in this genus based on the gene amplification results in Example 92. Coupled with the general knowledge in the art at the time of the invention, one skilled in the art knew to make and use the invention without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221*

USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Applicants also submit that the amendment to the specification incorporating the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent" should overcome the above rejection..

Hence, Applicants request that the present rejection to amended claims 39-58 be reconsidered and withdrawn.

5a) Claims 52-54 were rejected under 35 U.S.C. 112, second paragraph allegedly as being indefinite in reciting the terms "stringent hybridization conditions" without supplying specific conditions.

Claim 53 has been canceled without prejudice and hence this rejection is moot. Without admitting to the propriety of this rejection and solely in the interest of expediting prosecution in this case, Claim 52 has been amended to recite specific hybridization conditions performed "under stringent conditions," support for which can be found in the specification on page 73, line 34 to page 74, line 14, specifically on page 74, line 10-14. Claim 54 depends on amended claim 52. Applicants believe these amendments should overcome this rejection.

Thus, Applicants request that this rejection be withdrawn.

Claim rejection - 35 U.S.C. 102(b)

6a) Claims 39, 52-58 were rejected under 35 U.S.C. 102(b), allegedly, as being anticipated by Fuso Pharmaceuticals Ind. Ltd (WO 200031277; effective reference date 2/6/2000). Applicants respectfully traverse.

As discussed above, the effective reference date of the cited prior art is 2/6/2000 which is after the effective filing date of the present application, namely, December 16, 1999.

Thus, Applicants submit that Fuso is not proper prior art under § 102(b) and respectfully request withdrawal of this rejection.

Claim rejection - 35 U.S.C. 102(a)

6b) Claims 39-41, 52-54 were rejected under 35 U.S.C. 102(a), allegedly, as being anticipated by Yamaguchi (May 2001). Applicants respectfully traverse.

Again, the effective reference date of the cited prior art is 5/2001 which is after the effective filing date of the present application, namely, December 16, 1999.

Thus, Applicants submit that Yamaguchi is not proper prior art under §102(a) and respectfully request withdrawal of this rejection.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C80). Please direct any calls in connection with this application to the undersigned at the umber provided below.

Respectfully submitted,

Date: March 25, 2003

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